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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SOUAYA, JEHANNE E	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 05/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,478	SAKAKI, YOSHIYUKI	
	Examiner	Art Unit	
	Jehanne E Souaya	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *27 March 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-7,20,21 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *5 and 6* is/are allowed.

6)☒ Claim(s) *2-4,20,21 and 39* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7/2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *1449-10/2002*.

DETAILED ACTION

1. The examiner reviewing your application at the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to examiner Jehanne Souaya.

2. Currently, claims 2-7, 20, 21, and 39 are pending in the instant application. The rejections of claims 4, 20, and 21 under 35 USC 102 have been withdrawn in view of the amendments to the claims. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. The following rejections are either newly applied or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow.

Maintained Rejections

Claim Rejections - 35 USC § 103

3. Claims 4, 20, 21, and newly added claim 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kitamura et al in view of Nagase et al .

Kitamura et al. teach a DNA encoding rat Napl which is a protein which is 99.4% similar in amino acid sequence to the amino acid sequence of SEQ ID NO 2. Kitamura et al. teach that this DNA was isolated from rat brain tissue. The coding sequence is of identical length, i.e. 1128 amino acids, and is different at only 6 amino acids, 5 of which are conservative amino acid differences. The DNA of Kitamura et al. is 68% similar over all with regions of 91% similarity

to the nucleotide sequence of SEQ ID NO 1. The DNA of Kitamura et al., therefore is sufficiently similar to the DNA of SEQ ID NO 1 to hybridize under stringent conditions, and because of this very high degree of sequence similarity of the protein sequences can be reasonably assumed to have apoptosis suppressing activity. Kitamura et al. also taught that rat Napl was isolated by its ability to bind to human Nck protein known to be an oncoprotein. Kitamura et al. taught that binding proteins of the SH3 domains of Nck have been sought because of their suspected role is transmitting Res-dependent signals. (abstract).

The DNA of Kitamura et al. does not have 95% or more homology with the nucleotide sequence of SEQ ID NO 1 or the nucleotide sequence encoding SEQ ID NO 2. However, Kitamura et al. taught that rat Napl was isolated from rat brain cDNA using a mouse brain cDNA clone that had partial similarity to the rat Napl sequence as a probe in a colony hybridization assay (page 510, paragraph 2 and page 511, paragraph 2).

Furthermore, Nagase et al. teach the identification of coding sequences in human brain cDNA libraries by selecting clones having unidentified sequences at both termini and clones which produced proteins of 50 kDa or more in in vitro transcription/translation systems. These clones were then sequenced.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the art at the time the invention was made to have substituted the rat brain cDNA library of Kitamura et al. with the human brain cDNA library of Nagase et al. and have substituted the mouse brain cDNA probe used by Kitamura et al. with the rat Nap 1 cDNA of Kitamura et al. in order to have achieved the expected benefit of isolating the human Napl DNA homolog of Kitamura's rat Napl DNA and thereby making the claimed invention as a whole. The ordinary artisan would have

been motivated to have used the rat Napl DNA as a probe to isolate the human Napl homolog because Kitamura et al. taught that Nck binding proteins were expected to be involved in ras mediated cancers. While it would NOT have been obvious to have obtained a nucleic acid consisting of SEQ ID NO 1, the claims are broadly drawn to DNAs which are 95% homologous to SEQ ID NO 1, which encompasses a large number of different nucleic acid sequences. The ordinary artisan would have had a reasonable expectation that a human homolog having a 95% similar sequence to SEQ ID NO 1 would be isolated using the rat Napl coding DNA as a probe because Kitamura et al. taught that regions of the Napl rat and mouse protein were sufficiently homologous to allow hybridization and because the rat Napl protein was able to bind to human Nck protein suggesting a high degree of similarity between rat and hump proteins.

Kitamura et al does not teach isolating rat Nap 1 protein from cells transformed with recombinant vector containing rat Nap 1 nucleic acid, however Kitamura et al does teach isolating rat Nap 1 protein (see para bridging pages 509-510). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made that rat Nap 1protien could be isolated from cells transformed with recombinant vector containing rat Nap 1 encoding nucleic acid. The ordinary artisan would have been motivated to isolate rat Nap 1 protein for the purpose of studying the biological activity of rat Nap 1 protein.

Response to Arguments

The response traverses the rejection. The response asserts that the rejection has no basis in law because whether or not an ordinary artisan would have been motivated to substitute Kitamura's rat brain cDNA library with Nagase's human brain library or to utilize rat napl

cDNA probe for a mouse brain cDNA probe is off point because the claims are directed to DNA which is a product and not structurally obvious from anything taught by Kitamura and Nagase does not provide any motivation to make any of the necessary changes to Kitamura to conform its DNA to meet the claimed 95% homology. The response cites In re Deuel (34 USPQ 1210 (Fed Cir. 1995). This argument as well as the cited case law have been thoroughly reviewed but were found unpersuasive. Firstly, while Kitamura teaches a method of isolating rat Nap 1 DNA, Kitamura also teaches the DNA itself and Nagase specifically teaches a human brain cDNA library, also containing DNA, which is different than the facts of In re Deuel where no nucleic acid sequences were provided in the rejection. Further, while Nagase does not teach to make the necessary changes to Kitamura, this was not the reason cited by the examiner as to why the claimed genus of nucleic acids was structurally obvious over the teachings of Kitamura in view of Nagase. As stated in the previous office action and reiterated above: "it would have been *prima facie* obvious to one of ordinary skill in the art at the art at the time the invention was made to have substituted the rat brain cDNA library of Kitamura et al. with the human brain cDNA library of Nagase et al. and have substituted the mouse brain cDNA probe used by Kitamura et al. with the rat Nap 1 cDNA of Kitamura et al. in order to have achieved the expected benefit of isolating the human Napl DNA homolog of Kitamura's rat Napl DNA and thereby making the claimed invention as a whole. The ordinary artisan would have been motivated to have used the rat Napl DNA as a probe to isolate the human Napl homolog because Kitamura et al. taught that Nek binding proteins were expected to be involved in ras mediated cancers". In carrying out the method of Kitamura in view of Nagase as recited above, the ordinary artisan would have obtained a genus of nucleic acids that would have contained

significant overlap with the large genus of nucleic acids encompassed by the claimed recitation of "95% homology." In In re Deuel, the courts held that a prior art disclosure of the amino acid sequence of a protein does not necessarily render particular DNA molecules encoding the protein obvious. In the instant case, the examiner never made the assertion that either the specific DNA sequence of SEQ ID NO 1 was obvious. The examiner expressly stated that the prior art of Kitamura in view of Nagase did not make the specific DNA sequence of SEQ ID NO 1 obvious. However, the instantly rejected claims are not drawn to any specific nucleic acid sequence but to a large genus of sequences. Furthermore, pertaining to *In Re Deuel*, while the court determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious, regarding structural or functional homologues, however, the court stated

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologues because homologues often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

The claimed oligonucleotides simply represent structural and functional homologues of the sequence taught by Kitamura et al, concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds in humans as well because Kitamura teaches that Nck binding protein were expected to be involved in ras mediated cancers.

The response also asserts that the examiner's rejection is without basis in fact as prior to the instant filed specification, the inhibitory effect on apoptosis was not known and therefore those of ordinary skill would not have been motivated to act in conformity with the Examiner's process. This argument has been thoroughly reviewed but was not found persuasive as the

rejection clearly sets forth that "Kitamura et al. taught that binding proteins of the SH3 domains of Nck have been sought because of their suspected role is transmitting Res-dependent signals". Further, as motivation for isolating the human homolog of rat Nap 1, the rejection set forth: "Kitamura et al. taught that Nck binding proteins were expected to be involved in ras mediated cancers". The rejection under 35 USC 103 is maintained.

New Grounds of Objection and Rejection

Claim Objections

4. Claims 7 and 39 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot refer to two sets of claims with different features. Further, multiply dependent claims can only recite dependency in the alternative. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2-4 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 2-4, do not sufficiently distinguish over nucleic acids as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v.*

Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated", for example. See MPEP 2105.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 4, 20-21, and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 4 is broadly drawn to a DNA which hybridizes to the nucleotide sequence represented by SEQ I D NO 1 under stringent conditions, which has 95% or more homology with the nucleotide sequence represented by SEQ ID NO 1 and encodes a protein having apoptosis suppressing activities. The specification, however, does not define or provide guidance as to which "apoptosis activities" are suppressed by the protein encoded by the claimed genus of nucleic acids. The recited function fails to provide one of skill in the art with any guidance as to which amino acid sequences are sufficient from the polypeptide encoded by SEQ ID NO 1 to maintain "apoptosis suppressing activities". The claimed genus of nucleic acids encompasses homologs and allelic variants of SEQ ID NO 1 from any source.

Apoptosis is a response to intracellular environment conditions. Mutations in many different types of proteins involved in the apoptosis pathway could result in either suppression or acceleration of apoptosis. The recitation of "apoptosis suppressing activities" does not make clear any specific biological pathways, or activities such that the skilled artisan would be able to determine which amino acids could be altered and still result in a protein with such "activities". The specification does not provide any specific assays to measure such unknown function. Further, the specification does not actually measure any "suppression" in apoptosis, but concludes that the sequence encodes a protein with such function because antisense DNA assays against SEQ ID NO 1 resulted in acceleration of apoptosis. The specification thus concludes that SEQ ID NO 1 is involved in "suppressing apoptosis" but is silent as to how or which "activities" are encompassed by this broad and undefined recitation. It is clear from the recitation of "activities" (plural), the protein encoded by SEQ ID NO 1 could be associated with any number of activities associated with apoptosis, however the specification does not provide any description of what such would be such that the skilled artisan would be able to envision which amino acids could be altered and still result in a protein with such an undefined function. The instant claims are different than those exemplified in the Written Description guidelines, example 8 because the claims in the guidelines were directed to ligases whose structure and function relating to specific structural portions of the protein are well known in the art. Further, the activity or function implied by the recitation of "a DNA ligase" is immediately apparent to the skilled artisan. Further, because the crystal structure of ligases had been available, and because the art contained a large amount of teaching and guidance as to specific positions and amino acids responsible for the function of a DNA ligase, there was a known correlation between

structure and function with regard to ligases. With regard to the instant case, the specification provides no teaching or description of any correlation between what structure of proteins encoded by a DNA with 95% homology to SEQ ID NO 1 would be responsible for the broad and undefined recitation of "apoptosis suppressing activities".

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NOS: 1 and 2, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d

1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

As claim 4 lacks sufficient written description, claims 20, 21, and 39, drawn to vectors, host cells, and methods of making a protein using such also lack sufficient written description.

Conclusion

8. Claim 7 is objected to. Claims 5 and 6 are free of the cited prior art. Although claims 2 and 3 are free of the cited prior art, they are rejected under 35 USC 101.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya
Patent examiner
Art Unit 1634
Jehanne Souaya
5/21/03